COVID-19 Evidence Accelerator Collaborative

Diagnostics Evidence Accelerator #10

Thursday*, August 6, 2020, 12:00-1:00PM ET*

Call Summary

Introduction to Diagnostics Evidence Accelerator Meeting 10

This week's Diagnostics Evidence Accelerator meeting consisted of 3 presentations.

1. HHS Guidance on Lab Data Reporting (Sara Brenner, FDA/CDRH)
2. Real World Analysis of Serology Dx (Rohit Vashisht, University of California Health System)
3. Preliminary Descriptive Analysis: COVID-19 Laboratory Diagnostics (Adem Albayrak and Elizabeth Eldridge, Health Catalyst)

HHS Guidance on Lab Data Reporting (Sara Brenner, FDA/CDRH)

In June 2020, HHS released a COVID-19 Laboratory Data Reporting Guidance under the CARES Act. The goal of this guidance is to identify key data elements that are necessary to make decisions at the federal, state, and local governmental levels in response to COVID-19. This guidance applies to all testing performed in CLIA labs and home-use setting and outlines the data elements for COVID-19 testing data submission to HHS. On July 31, 2020, there was an additional implementation guidance that was released, which allows laboratories to utilize the strategies set forth by HHS to code and enter the different data element required.

The federal government is attempting to harmonize data and combine data across different categories. There are data element categories that are required to be reported to the federal government, state government, and the ordering provider. All laboratories are required to report, however, the FDA/CDRH are aware that there are labs that are at different technological readiness levels. Their goal is to work with stakeholders to improve the public health IT infrastructure for this pandemic and the future. There are several tests that are being used in the community. They are hoping to harmonize test codes through the laboratory information system and that information to flow throughout the ecosystem where the information is being exchanged with hospitals and clinical providers.

CDRH is working with RADx to accelerate diagnostic development for COVID-19. The projects that are being funded are point of care, at home, and at anywhere testing. The purpose of the HHS COVID-19 laboratory reporting guidance is to help assure a rapid and thorough public health response to the pandemic; maximize the utility of RWE; contribute to the understanding of disease incidence and trend; and empower patients with access to personalized test results and guidance and knowledge to take action to protect their community.

This presentation led to an intriguing discussion. Some points that were raised during the discussion were as followed

- The Chicago Department of Health built a data hub which is aggregating data from hospitals in Chicago using an electronic lab reporting system and EHR data. There were concerns surrounding the data fields for order entry for HHS and the data quality and integrity surrounding that. To combat this issue, Chicago Department of Health is planning on implementing a survey on their patient portal, which they will merge and add as part of the data feed.
- Another issue with data collection is that there is a character limit for data fields when entering according to the HHS guideline, therefore, gathering data is going to be a longer process.
- Another issue is that there are facilities that are conducting tests, but the data is not being reported.
- There are many data elements that are not in the providers system, therefore the research community is harvesting data that is not transmitted, while simultaneously creating new data, which could introduce bias.
- Data collection introduces issues with data privacy; therefore, we have to be mindful of this when collecting data.

Real World Analysis of Serology Dx (Rohit Vashisht, University of California Health System)

Dr. Rohit Vashisht discussed the preliminary results from Project One. Project One looks at sensitivity of a positive serology test following a positive PCR test. Specifically, the research team is looking at how the sensitivity vary by serology test manufacturer; the timing of the positive serology result, including IgM, IgG and total antibody; and how does test sensitivity vary by age group, gender, race, ethnicity, severity of COVID-19, co-morbidity, geographic location, and high vs low prevalence area. They answered these questions using the RWD collected during routine care of individuals across UC Health System. Their data set, UC Health COVID Data Set (CORDS), consist of clinical information for over 189,000 patients that have received COVID-19 related care. They have over 502 million data points which consist of lab data, visit data, medications, conditions, and procedures associated with the patients. CORDS is overseen by Center for Data-driven Insights and Innovations (CDI2). More information on the data collected can be found on the UC Health System website.

As of August 4th, 2020, UC Health System has tested over 12,197 patients for SARS-CoV-2 IgG antibodies. UC Health System is in the process of obtaining manufacturer information corresponding to the antibody tests used. There is a 6.1% positivity rate for SARS-CoV-2 antibodies. There are more female tested compared to males and more White Americans tested compare to Asian Americans and Black Americans. Approximately 22.13% of Americans do not have a race recorded, but the UC Health System is in the process of acquiring that data.

The steps that they are taking to address Project One is to look at the patients that are tested for a viral RNA using PCR test first, and then looking at the patient's antibody test later in the process. To account for a patient being tested multiple time, UC Health System looks at the first positive result that the patient had for both the PCR test and antibody test. The assumption that they made is that patients that tested negative with the PCR test were not tested elsewhere as positive. UC Health System looked at the time to develop antibody response in the population since a PCR positive result. They are taking advantage of the variability in the number of days between PCR and serology testing. They are not serially sampling for serology across time in individuals. From their results, the median number of days

that the antibody test is ordered is 31 days. Patients that are testing negative for the antibody test are being tested after a median of 19 days and patients that are testing positive are being tested after a median of 34 days. Therefore, if clinicians are testing earlier, they are more likely to get negative results than testing later. When the results are distributed among gender, male produce a negative antibody response earlier than females. The sensitivity of the test improves as the time period between the 2 tests increases. There is no difference in test sensitivity between males and females. The data was distributed among age groups. UC Health System saw that the older a patient is, the longer it takes to develop an antibody response. The age group of 0-24 years develop an antibody response in 2 weeks whereas the age group of 74+ is only able to reach a 70% sensitivity throughout UC Health System's data.

Preliminary Descriptive Analysis: COVID-19 Laboratory Diagnostics (Adem Albayrak and Elizabeth Eldridge, Health Catalyst)

Health Catalyst is sourcing data from multiple data sources across the country. The data that Health Catalyst has on patients is the data that is required by the HHS guideline such as lab data, demographic data, clinical data, and medication history. They have approximately 610,384 patients with a SARS-CoV-2 NAAT or antibody test with any result. This amounts to 1,202,898 lab results. Within the 610,384 patients, they have 597,263 patients with interpretable results amounting to 889,778 lab data elements. They have 97,188 patients that have a positive NAAT result and 3,287 patients with a positive NAAT result that had an antibody test. Finally, Health Catalyst has 949 patients that have both positive NAAT and antibody test results. Health Catalyst took a random sample of 50 patients that had a positive NAAT and antibody test, and they saw that there is a lot of variability in the timeline for the test results.

From the Chat Box

- Intriguing articles were shared in the chat box. The links to those articles are as followed
    - Changes in the Number of US Patients With Newly Identified Cancer Before and During the Coronavirus Disease 2019 (COVID-19) Pandemic
    - Contributions of Liquid-Based (Papanicolaou) Cytology and Human Papillomavirus Testing in Co-testing for Detection of Cervical Cancer and Precancer in the United States
- It was suggested that as a surrogate for device identifier, the TradeName_Manufacturer can be used as suggested by the HHS guideline. However, a caller did state that they are in the middle of delineating this and will clarify this in the coming weeks.
- It was suggested that test reagents are low in stock, therefore, this will affect the performance of the diagnostic test. This will make it difficult assess the performance of the many tests that are being used.
- To address the unique identifier problem, it was suggested that for personal devices, the MAC address of the personal smartphone is an option, if it is not masked by spoofing software.
- A caller asked UC Health a question regarding the indeterminate and pending results and whether they are binned into the negative results. UC Health is binning the results right now. They are starting an effort to get to the titer levels.
- It was suggested for the data for the ages 20 and under to be separated into 5-year segments for a better view of the data.
- A researcher stated that they observed that patients in New York, New Jersey, and New England have a far higher likelihood of IgG seropositivity than patents in other states, possibly because of heavier exposure and longer exposure early on. Likewise, people testing in same household

have high concordance rate (the "second" household member is likely to test positive if first person tested positive.
- It was stated that the goal of Project One is to address positive NAAT results with the intent of looking at data surrounding NAAT negative results later.

Next Steps

- Join fellow researchers on August 11, 2020 at 10:30 for a DIA webinar called DIA DIRECT: Real-World Data to Inform COVID-19 Response: Collaborating in the COVID-19 Evidence Accelerator. The registration link is http://engage.diaglobal.org/20220P11-COVID-19-Webinar.html
- If researchers are interested in participating in Project One, they can contact Amar Bhat at abhat@reaganudall.org.
- Continue making the data connection and learn about test performance for the next meeting.

Next Meeting: Thursday August 13th, 2020 12-1 pm ET